Claims (clean version encompassing amendments)

What is claimed is:

1. (once amended) In a method of providing a mixture of DNA fragments enriched in fragments that are characteristic of a phenotype of interest, which method includes providing affected DNA in fragmented form and providing unaffected DNA in fragmented form, the improvement comprising:

   a) mixing the fragments of the affected DNA and the fragments of the unaffected DNA under hybridising conditions to form hybrids;

   b) recovering a mixture of hybrids that contain mismatches;

   c) recovering fragments of the affected DNA from the mixture of hybrids that contain mismatches.

2. (once amended) The method of claim 1 wherein the affected DNA is pooled DNA of one or more individuals who show the phenotype of interest, and the unaffected DNA is pooled DNA of one or more individuals who do not show the phenotype of interest.

4. The method of claim 1, wherein the affected DNA is DNA of one individual who shows the phenotype of interest, and the unaffected DNA is pooled DNA of a

complete set of ancestors who do not show the phenotype of interest.

5. The method of claim 1, wherein the affected DNA is DNA from cells of an individual that show the phenotype of interest, and the unaffected DNA is DNA from cells of the individual that do not show the phenotype of interest.

6. (once amended) The method of claim 1, wherein step b) is performed by use of a mismatch-binding protein.

7. (once amended) The method of claim 1, wherein either the fragments of the affected DNA or the fragments of the unaffected DNA are tagged by one member of a specific binding pair, and step c) is performed by using the other member of the specific binding pair.

8. The method of claim 7, wherein the fragments of the unaffected DNA are tagged with biotin, and step c) is performed by use of immobilised streptavidin.

9. (once amended) The method of claim 1, further comprising subjecting the mixture of DNA fragments enriched in fragments that are characteristic of the phenotype of interest to self-hybridisation to form duplexes and subsequently recovering the perfectly matched duplexes.

10. (once amended) The method of claim 1, further comprising mixing the mixture of DNA fragments enriched in fragments that are characteristic of the phenotype of interest with an excess of the fragments of the affected DNA under hybridisation conditions to form duplexes and subsequently recovering the perfectly matched duplexes.

11. (once amended) The method of claim 1, wherein each of the affected DNA and the unaffected DNA is provided in fragmented form by digestion with from 4 to 7 six-cutter restriction endonuclease enzymes together with from 0 to 50 four-cutter restriction endonuclease enzymes.

14. A method of making a set of arrays of fragments of DNA of interest, which method comprises;

a) selecting, from a set of n restriction endonuclease enzymes, a subset of r restriction endonuclease enzymes;

b) digesting genomic DNA with the subset of r enzymes;

c) ligating to the resulting fragments restriction-enzyme-cutting-site-specific adapters with unique polymerase chain reaction amplifiable sequences;

d) splitting the resulting fragments into r^2 aliquots;

e) amplifying each aliquot with two restriction-enzyme-specific primers;

f) forming an array of the r^2 aliquots of non-tagged amplimer strands; and

g) repeating steps a) to f) using one or more different subsets of r restriction endonuclease enzymes.

15. (once amended) The method of claim 14, wherein steps a to f) are repeated using each different subset of r restriction endonuclease enzymes to give (n!)/[(n-r)!r!] different arrays.

16. (once amended) The method of claim 14, wherein the n restriction endonuclease enzymes are selected from 4-cutters and 5-cutters and 6-cutters.

17. (once amended) The method of claim 14, wherein the n is 3 to 10 and r is 2 to 4.

18. The method of claim 17, wherein n = 6 and r = 3.

21. (once amended) A set of arrays produced by the method of claim 14, derived from a set of n = 6 six-cutter restriction endonuclease enzymes which are *BamHI*; *Bsr GI*; *Hind III*; *Ncol*; *Spel*; and *AflII*.

22. (once amended) A set of arrays produced by the method of claim 14, derived from the set of n = 6 six-cutter restriction endonuclease enzymes which are *EcoRI*; *BspHI*; *BglII*; *Xbal*; *Acc65I*; and *ApaLI*.

23. (once amended) A nucleic acid characterisation method which comprises presenting to a set of arrays produced by the method of claim 14 a nucleic acid fragment of interest under hybridisation conditions, and observing a pattern of hybridisation.

24. The method of claim 23, wherein a plurality of nucleic acid fragments of interest are separately presented to the set of arrays, and the resulting patterns of hybridisation are compared.

25. The method of claim 24, wherein the plurality of nucleic acid fragments of interest are drawn from the mixture of DNA fragments, enriched in fragments that are characteristic of a phenotype of interest, of claim 13.

27. A double-stranded DNA molecule having the sequence a-A-b-B...X-y-Y-z where A, B...X and Y are unique restriction sites for n different restriction endonuclease enzymes, and a, b...y, z denotes distances in base pairs, characterised in that each fragment, obtainable by cutting the DNA molecule by means of any one or more up to n of the restriction enzymes, has a different length from every other fragment.

28. (once amended) The double-stranded DNA molecule of claim 27, wherein:

a) inter-fragment length differences are greater for larger fragments;

b) all possible fragments are unambiguously resolvable by electrophoresis from one another;

c) size gaps between bands comprising different numbers of inter-restriction-site units are larger than size gaps between bands comprising the same number of inter-restriction-site units;

d) the size gaps and size spread from the largest to the smallest fragment are electrophorectically compatible.

29. (new) The method of claim 1 which further comprises steps a), b) and c) one or more times.

30. (new) The method of claim 14 wherein one of the restriction enzyme specific primers is tagged.